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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,780	11/17/2000	Helene Gras-Masse	1091/2 PCT/US	9478

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,780	GRAS-MASSE ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *8,12 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-11 and 13-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The request filed on April 5, 2004 for a Request for Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/555,780 is acceptable and a RCE has been established. An action on the RCE follows.

In the paper submitted April 5, 2004, applicant amended claim 1. Claims 1-25 are pending, claims 8 and 12 are withdrawn from consideration due to a non-elected invention. It is noted that the subject matter of claim 25 also encompasses the non-elected and withdrawn subject matter of claim 8. It is also noted that the previous Office action inadvertently listed claim 25 in the rejection headers, even though the limitations of the claim were never addressed. Since claim 25 encompasses the subject matter of claim 8, which was withdrawn from consideration, claim 25 is also withdrawn from consideration due to a non-elected invention. Therefore, claims 1-7, 9-11 and 13-24 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13, 14, 16 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for reasons of record.

Applicant asserts that the disclosures of Pialoux et al. and Gahery-Segard et al. (provided with the response of 12/4/01) provide ample evidence to one skilled in the medical arts that the instant micelles are functional in inducing the immune response claimed. Applicant points to exhibits 1 and 2. The first is an article by the present inventors (Gahery-Segard et al.), demonstrating that the claimed compounds induce a long-term CD8+ reactive immune response against HIV. Applicant also points to the teachings of Levy et al. in exhibit 2. Applicant asserts that the conclusions of these teachings indicate that the claimed vaccine compositions are active against HIV.

Applicant's arguments as well as a full review of the references submitted have been considered, but are found unpersuasive. The instant claims require a vaccine and a method of immunizing against any pathogen, but the nature of the invention is directed to a vaccine against HIV. A vaccine is required to have ameliorative properties against infection and/or preventative properties against possible infections by definition. Since the predictability in the HIV vaccine art is extremely low, applicant is required to provide evidence of the claimed effectiveness of the vaccine claimed.

The working examples show limited antibody responses generated in normal individuals upon administration of the micelle compositions, see pages 25-28. There are also examples of *in vitro* proliferation experiments, which were shown to be limited to PBMC proliferation, see page 30, second paragraph through page 32. There are no working examples demonstrating therapeutic or protective efficacy of the vaccine claimed.

The teachings of Levy et al., discussed by applicant, conclude that HIV replication is better controlled after stopping HAART and upon administration of

ALVAC-VIH 1433 and HIV lipopeptides. However, better control of HIV replication does not indicate amelioration of disease. In addition, the HIV replication concluded by Levy et al. cannot be completely attributable to the HIV lipopeptides alone since the reference teaches simultaneous administration of ALVAC-VIH 1433 and HIV lipopeptides. In contrast, the teachings of Gahery-Segard et al. show a long-term immune response upon administration of an anti-HIV lipopeptide composition. However, since the immune responses observed by Gahery-Segard et al. were in healthy, HIV seronegative individuals, there can be no correlation made between the immune responses observed in healthy individuals and HIV-infected patients with impaired immune systems.

Desrosiers (Nature Medicine. March, 2004; 10 (3): 221-223) reviews the current state of the HIV vaccine art and provides several explanations for the lack of development of an HIV vaccine. These include the ineffectiveness of the natural immune response to infection, the lack of an animal model, the inability to protect related primates from similar viruses, the lack of protection against heterologous viral infection and the resistance of HIV to neutralization in a phase 3 vaccine trial. Desrosiers states that it is currently unknown what kind of an immune response would be effective against infection, how to elicit neutralizing antibodies against the virus or how to overcome obstacles due to HIV sequence variability.

It is beyond one skilled in the art to use the vaccine composition claimed in a pharmaceutical composition to induce a therapeutic or prophylactic immune response because there is no disclosure provided for how one would overcome the current obstacles in the HIV vaccine art, discussed by Desrosiers.

The assertion of therapeutic and prophylactic requirements necessarily requires evidence to support applicant's assertion. Since the art does not disclose any ameliorative or preventive HIV agents, the skilled artisan would not predict, in the absence of proof to the contrary, that the micelle composition instantly claimed would be efficacious as an HIV vaccine, or a vaccine possessing therapeutic and protective properties against any and all pathogens.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). There is not seen in the disclosure, sufficient evidence to support the instant claims of prevention or treatment of HIV or any pathogen with the instant micelle composition. There are also no working examples or data in the art that would provide a nexus between the effectiveness of the instant composition and an HIV vaccine. For these reasons, it is determined that the instant claims would require an undue quantity of experimentation of one skilled in the art to make and use the invention claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 9-10, 13-17, 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stuhler et al., Sastry et al. and Sugimoto et al. for reasons of record.

Applicant points out that claim 1 has been amended to state that the claimed composition comprises more than one first lipopeptide comprising at least one CTL antigenic determinant and at least one lipid unit. Applicant argues that the prior art cited does not teach or suggest the essential technical feature of the invention since Sastry et al. only disclose administering a single immunogenic peptide. Applicant also points to Gahery-Segard et al. and Levy et al., supra, and example 4 in the specification showing induction of a multiepitopic CTL response.

Applicant's arguments have been fully considered, but are found unpersuasive. The deficiencies in the teachings of Gahery-Segard et al. and Levy et al. are discussed above. Contrary to applicant's assertions, Sastry et al. do teach administering more than one lipopeptide comprising at least one CTL antigenic determinant and at least one lipid unit. Sastry et al. teach eliciting cell-mediated immunity with micelles comprising short HIV envelope peptides of gp160 with two palmitic residues attached to the amino-terminal lysine. Sastry et al. generates these micelle compositions by dissolving the peptides with the palmitic residues attached in acetic acid, see the abstract and "peptide polymers" on page 700. Therefore, Sastry et al. teach a composition comprising more than one lipopeptide comprising at least one CTL antigenic determinant and at least one lipid unit. Although the peptides generated by Sastry et al. are derived from a single gp160 protein from HIV, the peptides derived from it contain more than one CTL determinant. One of ordinary skill in the art at the time the invention was made would have been motivated to present various portions of a protein in the form of peptides, as

Sastry et al. do, to ensure that the immune system is uniformly presented with a complete set of epitopes from the antigenic peptide.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stuhler et al. and Sastry et al. and Sugimoto et al. as applied to claims 1-7, 9-10, 13-17, 19-24 above, and further in view of Kramer et al. for reasons of record.

Applicant asserts that claim 11 is patentable for the same reasons presented in the arguments section regarding claim 1. However, as discussed above, these arguments are not sufficient to overcome the rejection of record and the instant rejection of claim 11 is maintained for reasons of record.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stuhler et al., Sastry et al., Sugimoto et al., and Kramer et al. as applied to claims 1-7, 9-11, 13-17, 19-24 above, and further in view of Shapiro et al. for reasons of record.

Applicant argues that the teachings of Kramer et al. fail to remedy the defects of Stuhler et al., Sastry et al. and Sugimoto et al. However, as discussed above, there are no defects in the combination of teachings of Stuhler et al., Sastry et al. and Sugimoto et al. Therefore, the rejection is maintained for reasons of record.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley
Patent Examiner, 1648